

Atty. Dkt. No. 025098-0701

Listing of the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously presented) A method for designing a specific polyamide



wherein

X_1 , X_2 , X_m , $X_{(m+1)}$, $X_{(2m-1)}$, and X_{2m} are carboxamide residues forming carboxamide binding pairs X_1/X_{2m} , $X_2/X_{(2m-1)}$, $X_m/X_{(m+1)}$,

γ is γ -aminobutyric acid or 2,4 diaminobutyric acid, and

R_1 is $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$, $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$, or $-\text{NHR}_2$, where R_2 and R_3 are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl, C_{1-100} alkyl, C_{1-100} alkylamine, C_{1-100} alkyldiamine, C_{1-100} alkylcarboxylate, C_{1-100} alkenyl, a C_{1-100} alkynyl, and C_{1-100} alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosoarea, fluorescein, bromoacetamide, iodoacetamide, DL- α -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- α -tocopheral, suitable for use as a DNA-binding

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ligand that is selective for identified target DNA-sequences $5'\text{-WN}_1\text{N}_2 \dots \text{N}_m\text{W-3'}$ where m is an integer having a value from 3 to 6, the method comprising:

(a) identifying a target sequence of double stranded DNA having the form $5'\text{-WN}_1\text{N}_2 \dots \text{N}_m\text{W-3'}$, $\text{N}_1\text{N}_2 \dots \text{N}_m$ being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;

(b) representing the identified sequence as $5'\text{-Wab} \dots x\text{W-3'}$, wherein a is a first nucleotide to be bound by the X_1 carboxamide residue, b is a second nucleotide to be bound by the X_2 carboxamide residue, and x is the corresponding nucleotide to be bound by the X_m carboxamide residue;

(c) defining a as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d) selecting Im as the X_1 carboxamide residue and Py as the X_{2m} carboxamide residue if $a = \text{G}$;

(e) selecting Py as the X_1 carboxamide residue and Im as the X_{2m} carboxamide residue if $a = \text{C}$;

(f) selecting Hp as the X_1 carboxamide residue and Py as the X_{2m} carboxamide residue if $a = \text{T}$;

(g) selecting Py as the X_1 carboxamide residue and Hp as the X_{2m} carboxamide residue if $a = \text{A}$; and

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(h) repeating steps c – g for *b* through *x* until all carboxamide residues are selected; wherein Im is N-methylimidazole, Hp is 3-hydroxy-N-methylpyrrole, Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine; and synthesizing the polyamide.

2. (Cancelled)

3. (Previously presented) The method of claim 1 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

4. (Previously presented) The method of claim 1 further comprising the step of determining if the polyamide exhibits a binding affinity that is at least ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

5. (Previously presented) The method of claim 1 further comprising the step of replacing at least one pyrrole residue with a β -alanine residue.

6-37 (Cancelled)

38. (Previously presented) A polyamide composition produced by the method of claim 1 wherein one carboxamide binding pair is β/β , wherein β is β -alanine.

39-41. (Cancelled)

42. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a regulatory sequence.

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43. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a promoter sequence.

44. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a coding sequence.

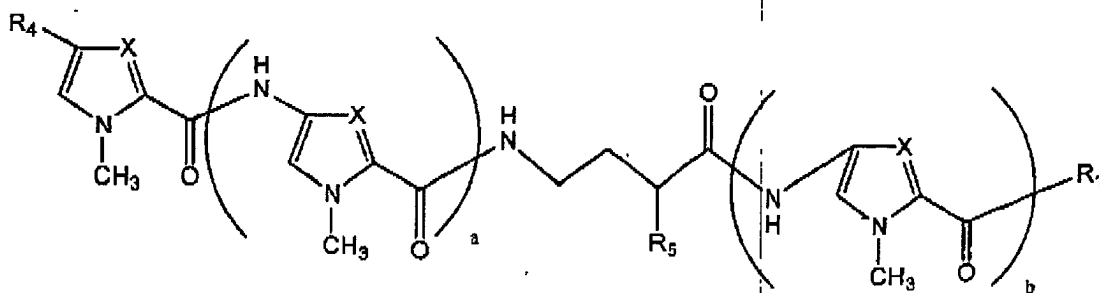
45. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a non-coding sequence.

46. (Previously presented) A polyamide composition produced by the method of claim 1 wherein the binding of the carboxamide binding pairs to the identified target DNA sequence modulates the expression of a gene.

47. (Previously presented) A composition comprising an effective amount of a polyamide produced by the method of claim 1 and a pharmacologically suitable excipient.

48. (Previously presented) A diagnostic kit comprising a polyamide produced by the method of claim 1.

49. (Previously presented) A polyamide designed by the method of claim 1, having the structure:



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wherein

R_4 is selected from the group consisting of H, NH_2 , SH, Cl, Br, F, N-acetyl, and N-formyl;

R_5 is H or NH_2 ;

R_1 is $-NH(CH_2)_{0-100}NR_2R_3$, $-NH(CH_2)_{0-12}CONH(CH_2)_{0-100}NR_2R_3$, or $-NHR_2$, where R_2 and R_3 are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl, C_{1-100} alkyl, C_{1-100} alkylamine, C_{1-100} alkyldiamine, C_{1-100} alkylcarboxylate, C_{1-100} alkenyl, a C_{1-100} alkynyl, and C_{1-100} alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- α -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrnilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- α -tocopheral;

each X is independently selected from the group consisting of N, CH, and COH;

each a is an integer from 2 to 5; and

each b is an integer from 3 to 6.